Tropical Medicine and International Health doi:10.1111/j.1365-3156.2007.01982.x

VOLUME 13 NO 1 PP 129–138 JANUARY 2008

# Ascertainment of childhood vaccination histories in northern Malawi

**A. Jahn[1,2], S. Floyd[2], V. Mwinuka[1], J. Mwafilaso[1], D. Mwagomba[3], R. E. Mkisi[3], A. Katsulukuta[4], A. Khunga[5], A. C. Crampin[1,2], K. Branson[2], N. McGrath[1,2] and P. E. M. Fine[2]**

1 *Karonga Prevention Study, Chilumba, Malawi*
2 *Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK*
3 *The Zonal Health Support Office, Mzuzu, Malawi*
4 *Ministry of Health and Population, Lilongwe, Malawi*
5 *Karonga District Hospital, Karonga, Malawi*

**Summary**

OBJECTIVE To assess factors related to recorded vaccine uptake, which may confound the evaluation of vaccine impact.

METHODS Analysis of documented vaccination histories of children under 5 years and demographic and socio-economic characteristics collected by a demographic surveillance system in Karonga District, Malawi. Associations between deviations from the standard vaccination schedule and characteristics that are likely to be associated with increased mortality were determined by multivariate logistic regression.

RESULTS Approximately 78% of children aged 6–23 months had a vaccination document, declining to <50% by 5 years of age. Living closer to an under-5 clinic, having a better educated father, and both parents being alive were associated with having a vaccination document. For a small percentage of children, vaccination records were incomplete and/or faulty. Vaccination uptake was high overall, but delayed among children living further from the nearest under-5 clinic or from poorer socio-economic backgrounds. Approximately 9% of children had received their last dose of DPT with or after measles vaccine. These children were from relatively less educated parents, and were more likely to have been born outside the health services.

CONCLUSIONS Though overall coverage in this community was high and variation in coverage according to child or parental characteristics small, there was strong evidence of more timely coverage among children from better socio-economic conditions and among those who lived closer to health facilities. These factors are likely to be strong confounders in the association of vaccinations with mortality, and may offer an alternative explanation for the non-specific mortality impact of vaccines described by other studies.

**keywords** vaccine uptake, vaccine impact, confounders, parental characteristics, Malawi

## Introduction

The WHO Expanded Programme on Immunization (EPI) was initiated in 1974 to promote immunization for all children with a basic schedule of BCG and OPV at birth or first contact; DPT and OPV at 6, 10 and 14 weeks, and measles at 9 months (WHO 2001, 2003). Global coverage is now approximately 90%. Following WHO recommendations many countries have added Hepatitis B (HepB) and other vaccines. Schedules have been questioned in terms of optimal immune response and disease reduction, and also in relation to other paediatric services such as growth monitoring and micronutrient supplementation (WHO 2006). Unexpected, non-target disease-specific effects of vaccines have been reported, related to age at and order of vaccination (Kristensen *et al.* 2000), e.g. detrimental effects associated with DPT administered simultaneously or after measles vaccine (Aaby *et al.* 2003). Other studies have not confirmed these findings (Fine 2000; Breiman *et al.* 2004; Global Advisory Committee on Vaccine Safety 2004; Vaugelade *et al.* 2004; WHO Task Force on Routine Infant Vaccination and Child Survival 2004; Elguero *et al.* 2005; Lehmann *et al.* 2005; Moulton *et al.* 2005).

The EPI uses standardized monthly reports to monitor vaccination coverage and target disease incidence. Coverage estimates are based on the ratio of the number of

vaccine doses administered to a 'target population' (1/12th of under 1-year-olds living in the catchment area of a 'static' health facility). Additional national coverage surveys are conducted periodically, reviewing vaccination histories of a sample of seven children aged 12–23 months in 30 randomized household clusters (Expanded Programme on Immunization 1991; Hoshaw-Woodard 2001). These standard coverage estimates are insufficient for detailed analysis of vaccination effects, due to lack of socio-economic data that are likely to confound impact assessment.

We studied availability and content of child-held vaccination documents in northern Malawi to assess uptake, timeliness and order of vaccinations and their association with background characteristics in order to further inform the debate about possible non-specific effects on child survival.

Karonga is a rural district bordering Tanzania in northern Malawi. The population of 236 000 relies mainly on subsistence farming and fishing. BCG and DPT were introduced by mobile teams in the mid-1970s; the Malawi EPI programme started in 1979. Malawi's vaccines are procured through UNICEF and distributed from central to regional to district cold stores. Karonga has 20 'static' vaccination facilities that run vaccination clinics once or twice weekly. Each facility additionally operates several monthly outreach clinics (92 in total). The Malawi schedule follows the EPI standard schedule, except that measles vaccination is recommended from age 10 months (Malawi Ministry of Health and Population 2002). Repeat BCG is recommended if a scar fails to form after 6 weeks. If OPV or DPT are started late, the guidelines emphasize the importance of the minimum interval of 4 weeks for subsequent doses. *Haemophilus influenzae* B (Hib) and HepB vaccines were introduced as a pentavalent vaccine (DPT + HepB + Hib) in January 2002, given as a single injection (Malawi Ministry of Health and Population 2002).

Until 2001, a free child health card was issued to all children on their first visit to a health facility. This included space to record vaccinations, a growth chart and basic clinical notes. A new patient-held 'health passport' was introduced in 2002. Financed by a revolving fund, the document must be purchased by patients, for the equivalent of $0.15. The fee is intended as an incentive to keep the passport safe. It includes a page for type, dose and date, but not place of vaccination.

Malawi has held periodic vaccination campaigns for measles (1998, 2002, 2005) and polio (1996, 1997), targeting children of particular age ranges (e.g. for measles, in 1998 children under 15 years and in 2005 children under 5 years), regardless of their previous vaccination status. Neither these additional doses nor repeat BCG vaccinations are typically recorded in vaccination documents.

## Methods

Data were collected during the initial census for a demographic surveillance system (the Karonga Continuous Registration System, CRS), covering 4% (135 $km^2$) of the district and 13% (31 000) of the population (A. Jahn *et al.* 2007). The catchment areas of all health facilities in the district have been geographically defined as contiguous zones by the Health Management Information System of the Ministry of Health. The CRS area overlaps with the catchment areas of one rural hospital and three health centres (one fully, three partly) that operate a total of 14 under 5 outreach clinics within the CRS area (Figure 1).

Trained interviewers visited every household between 21 August 2002 and 22 July 2004, recording GPS coordinates and socio-economic household data, such as sources of income, household assets and housing standard, classified by construction materials and availability of electricity and piped water. Socio-demographic details were collected for all household members. Data on under 5-year-olds included date and place of birth, sex, vaccination history and parents' identity. Field staff requested health documents for all under 5-year-olds, transcribing vaccination types and dates onto questionnaires. Only recorded data on vaccinations were considered, including those in health passports, child health cards and improvized documents (e.g. exercise books, scrap paper). Date of birth was ascertained from health documents whenever available. If not available in writing, birth dates were obtained as precisely as possible from a parent or other adult household member. Staff examined the right upper arm of all household members for signs of a BCG lesion or scar. Only lesions classified as 'clear and typical' BCG scars were considered.

Ethical approval was obtained from the Malawi National Health Sciences Research Committee and the Ethics Committee of the London School of Hygiene & Tropical Medicine. Informed consent was obtained from all study subjects or legal guardians.

Data were double entered and checked for consistency. Implausible date sequences for repeated doses of OPV and DPT and inconsistencies between birth date, vaccination and interview dates were referred to the field. For data description, age at interview was calculated using date midpoints if month and/or day of birth were unknown. Children without complete birth date were excluded from analyses of age at vaccination.

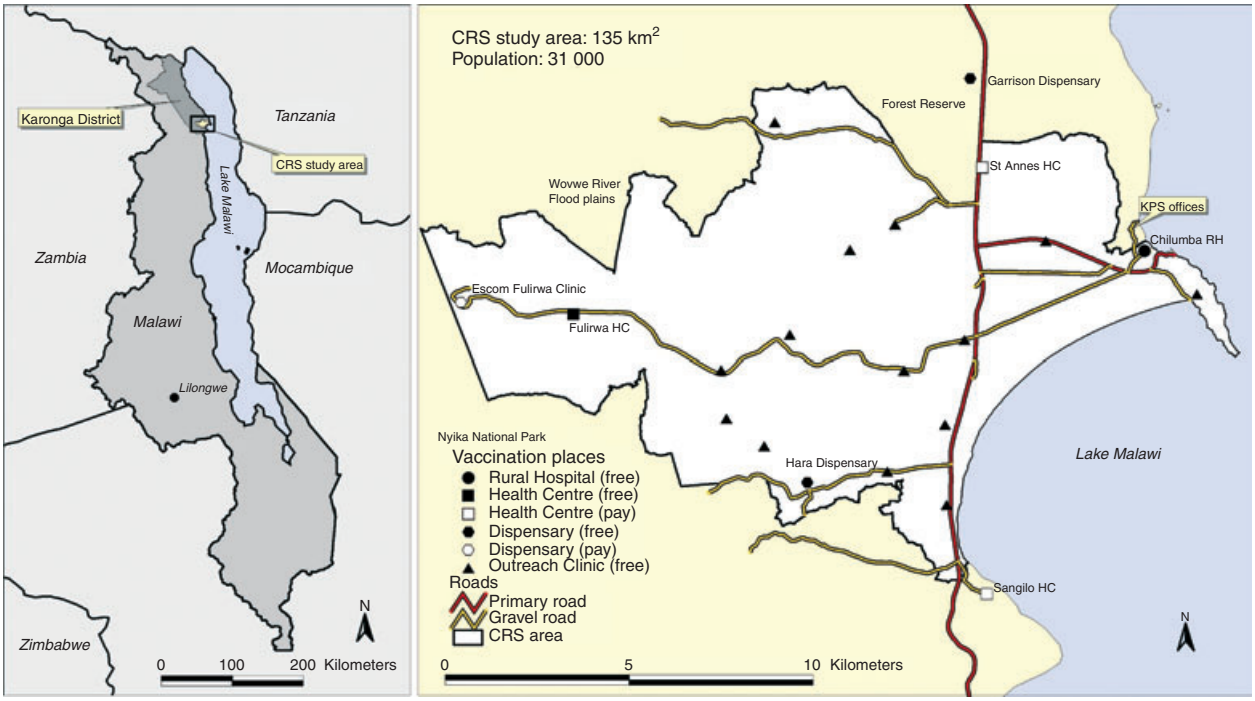


**Figure 1** Map of Karonga District showing CRS area, Chilumba Rural Hospital (CRH), local health centres (At Anne's Fulirwa, Sangilo) and outreach clinic sites. Health facilities marked as 'pay' charge for under-5 clinic services though EPI vaccinations are provided free of charge at all facilities.

Analyses of distributions were carried out using proportions and histograms. Associations between background characteristics and vaccination outcomes were analysed using odds ratios (ORs) and 95% confidence intervals (CI) for ORs. Multivariate logistic regression was used to quantify the effects of multiple characteristics simultaneously. Vaccination coverage by age was modelled using the Kaplan–Meier failure function, treating completion of vaccination as the 'failure event'. Children were entered into the analysis at birth and observations were censored at the time of review of the vaccination documents. Distances between households and the nearest respective under-5 clinic were calculated as straight lines, performing a *spatial join* between all household and clinic coordinates in *ArcView 3.1*. Based on the observed distribution of distances and assuming that access to clinics was almost exclusively by foot, the following thresholds were considered relevant: <1 km; 1 to <1.5 km; ≥1.5 km. Analyses that allowed for clustering of children due to sharing the same parents and/or household gave virtually identical results to the 'uncorrected' analyses, and the results from the latter are presented.

## Results

In total, 29 923 individuals were recruited in the baseline census. Accepting midpoints for unknown birth month and/or day, 5418 children born between September 1997 and June 2004 were eligible. For 671 (12%) children, only the year of birth could be obtained; for 912 (17%) the birth month and for 3835 (71%) the precise birth date was available.

Table 1 shows availability of vaccination documents and precise birth dates, by interview age. Of 5418 children, vaccination documents were available for review for 3440 (63%). Children aged 6–23 months were most likely to have a document (78%). Those with documents were more likely to have a known precise birth date [OR: 3.29 (2.92–3.72)]. More than 20% of vaccination documents did not display a precise birth date. Younger children, girls and non-orphans were more likely to have a known precise birth date [OR for every year increase in age = 0.77 (0.49–0.91), OR girls *vs.* boys = 1.15 (1.02–1.31), OR non-orphans *vs.* orphans = 1.49 (1.10–2.03); adjusted ORs, controlled for availability of a document].

**Table 1** Known precise date of birth (DOB) and available vaccination documents by age at interview and by sex

| Interview age | *n* | With precise DOB | With vaccination document | With precise DOB and vaccination document |
|---|---|---|---|---|
| Boys | | | | |
| 0–5 months | 352 | 284 (81%) | 226 (64%) | 192 (55%) |
| 6–11 months | 316 | 237 (75%) | 239 (76%) | 191 (60%) |
| 12–23 months | 621 | 470 (76%) | 480 (77%) | 397 (64%) |
| 24–35 months | 550 | 373 (68%) | 361 (66%) | 282 (51%) |
| 36–47 months | 525 | 328 (62%) | 295 (56%) | 222 (42%) |
| 48–59 months | 415 | 250 (60%) | 181 (44%) | 130 (31%) |
| Boys <5 years | 2779 | 1942 (70%) | 1782 (64%) | 1414 (51%) |
| Girls | | | | |
| 0–5 months | 317 | 264 (83%) | 202 (64%) | 173 (55%) |
| 6–11 months | 315 | 259 (82%) | 254 (81%) | 217 (69%) |
| 12–23 months | 539 | 407 (76%) | 417 (77%) | 341 (63%) |
| 24–35 months | 530 | 362 (68%) | 350 (66%) | 270 (51%) |
| 36–47 months | 554 | 359 (65%) | 280 (51%) | 214 (39%) |
| 48–59 months | 384 | 242 (63%) | 155 (40%) | 122 (32%) |
| Girls <5 years | 2639 | 1893 (72%) | 1658 (63%) | 1337 (51%) |
| Boys and girls <5 years | 5418 | 3835 (71%) | 3440 (63%) | 2751 (51%) |

Table 2 shows univariate associations of socio-demographic characteristics with possession of a vaccination document. Crude ORs are presented as they altered very little after adjustment for other factors. Although children lived up to 14.3 km from the main road, all lived within a 3.8 km radius of an under-5 vaccination (outreach) clinic. In univariate analysis, children living closer to a clinic and with better educated parents were significantly more likely to have vaccination documents [OR for mothers in the lowest education category: 0.79 (0.66–0.94); OR for fathers in the highest education category: OR 1.20 (1.04–1.37)]. Orphans, particularly maternal orphans, were less likely to have a vaccination document than non-orphans. There was no association with housing standard.

Table 3 documents the association between BCG scar, availability of vaccination document and written evidence of BCG vaccination. The percentage with a scar increased with age, and was highest amongst those with recorded BCG vaccination (78%), lowest in those without recorded BCG vaccination (50%) and intermediate in those with no document (70%). The proportions of children with a scar who also had a record of BCG vaccination were similar for the eight birth year cohorts 1997–2004 (91–97%).

The BCG scar data allow inference of population vaccination coverage independently from vaccination records. BCG coverage was expected to be lower in children without documents, yet the scar rate of 70% suggests that most of them had received BCG. We therefore calculated inferred BCG coverage in children aged 12–59 months (excluding the youngest group as recent vaccinations may lead to unreliable scar reading). Among 833 without document, 626 (75%) had a BCG scar (Table 3, data in bold). Of 1687 children with documented BCG vaccination, 1327 (79%) had a scar (Table 3, data in italics). Assuming the same probability of BCG scar formation in children with and without document, BCG coverage in the group without documents is very high (75% ÷ 79% = 95%).

General vaccine coverage in 2460 children with document who were at least 12 months at review (including those with incomplete birth dates) was: BCG 94%, OPV0 24%, OPV1 96%, OPV2 95%, OPV3 92%, DPT1 96%, DPT2 95%, DPT3 90% and measles 89%. Coverage was lower in children with less educated mothers, poorer housing and living further from the nearest under-5 clinic, with differences among categories ranging between 2% and 10% (results not shown).

Age at vaccination was calculated for 2751 children with vaccination document and precise known birth date. Sixty-nine children were excluded from analyses because the recorded date of first vaccination was before the birth date.

Figure 2a–c shows the distribution of ages at vaccination. Cumulative coverage for each vaccine by age was estimated using the Kaplan–Meier method. BCG coverage was 22%, 53% and 81% by 1, 6 and 14 weeks of age, respectively, with a final coverage of 95% at 15 months. Only 2% of infants had received DPT3 by the recommended age of 14 weeks, 49% were vaccinated by 6 and 76% by 9 months, and maximum DPT3 coverage (92%) was reached by 23 months. For measles vaccine, recommended in Malawi from 10 months, 17% were vaccinated before 9 months and 48%, 75% and 86% of children were

vaccinated by 10, 12 and 18 months, respectively. Final coverage of 92% was reached by approximately 4 years of age.

**Table 2** Univariate analysis showing factors related to the availability of a vaccination document for review at the census visit

| | Total/*n* | Children with vaccination document | Crude OR |
|---|---|---|---|
| Total | 5418 | | |
| Place of birth | | | |
| Health facility | 3638 | 2410 (66%) | Ref. |
| TBA camp | 474 | 323 (68%) | 1.09 (0.88–1.34) |
| Home | 1010 | 674 (67%) | 1.02 (0.88–1.18) |
| Distance to nearest U5-clinic | | | |
| 0 km | 3146 | 2045 (65%) | Ref. |
| 1 km | 1309 | 832 (64%) | 0.94 (0.82–1.07) |
| 1.5 km | 949 | 553 (58%) | 0.75 (0.65–0.87) |
| Housing standard | | | |
| 6 (highest) | 174 | 107 (61%) | 1.03* (0.99–1.08) |
| 5 | 185 | 111 (60%) | |
| 4 | 937 | 596 (64%) | |
| 3 | 2022 | 1262 (62%) | |
| 2 | 945 | 622 (66%) | |
| 1 (poorest) | 1111 | 715 (64%) | |
| Orphanhood | | | |
| Non-orphan | 5088 | 3278 (64%) | Ref. |
| Paternal orphan | 152 | 81 (53%) | 0.63 (0.46–0.87) |
| Maternal orphan | 37 | 14 (38%) | 0.34 (0.17–0.65) |
| Double orphan | 6 | 1 (17%) | 0.11 (0.01–0.95) |
| Mother's education | | | |
| <5 years primary | 634 | 385 (61%) | 0.79 (0.66–0.94) |
| Primary 5+ | 3585 | 2373 (66%) | Ref. |
| Sec./tert. | 868 | 572 (66%) | 0.99 (0.84–1.15) |
| Father's education | | | |
| <5 years primary | 322 | 204 (63%) | 0.93 (0.73–1.18) |
| Primary 5+ | 2361 | 1535 (65%) | Ref. |
| Sec./tert. | 1548 | 1068 (69%) | 1.20 (1.04–1.37) |

*OR for a one-unit change in category assuming a linear trend.

Estimated full vaccination coverage by age is displayed in Figure 3. Coverage by 12 months was 67%, 80% were fully vaccinated by 18 months and final coverage was 86% (95% CI: 84–88%) at 36 months of age. Table 4 describes children who had completed BCG, DPT3, OPV3 and measles vaccine before their first birthday [defined by the Malawi EPI programme as 'fully protected' children (Malawi Ministry of Health and Population 2002)]; 67% of children reached this goal, both amongst the 2744 children with precise birth date and valid vaccination dates and in the subgroup of 1978 children with information on all background characteristics.

Birth place, distance to nearest under-5 clinic, housing standard and mother's education were significantly associated with vaccination coverage in univariate analyses (Table 4). In the adjusted model, home-born children were not significantly less likely to be 'fully protected' [adjusted OR: 0.88 (0.68–1.12)]. However, children whose mothers had chosen a traditional birth attendant camp remained less likely to be 'fully protected' [adjusted OR: 0.67 (0.49–0.93)].

Children living in poorer housing were less likely to be 'fully protected' [93% in the top category *vs.* 61% in the lowest; adjusted OR for every unit decrease in housing score ranging from 6 to 1 = 0.87 (0.79–0.95)]. Mothers with secondary or higher education had 77% 'fully protected' children *vs.* 59% for those with <5 years primary education [adjusted OR for a one-unit increase in educational category = 1.30 (1.07–1.58)]. Children who lived further from the nearest under-5 clinic were less likely to be 'fully protected' [70% living within <1 km *vs.* 57% living ≥1.5 km; adjusted OR for 0.5 km increase = 0.81 (0.71–0.93)].

Figure 4 shows timing between measles and the last DPT vaccination. Of 2381 children with documented evidence of having received at least one dose of DPT and measles vaccine, 11% received measles vaccine simultaneously with or before their last dose of DPT. Among these, 2359

**Table 3** Proportion of children with definite evidence of a BCG scar (restricted to children examined for BCG scar), by age at interview and availability of a vaccination document with or without recorded BCG vaccination

| | Total | No document | | Document but no BCG recorded | | Document and BCG recorded | |
|---|---|---|---|---|---|---|---|
| Interview age | *n* | *n* | With scar | *n* | With scar | *n* | With scar |
| 0–11 months | 858 | 143 | 54 (38%) | 34 | 10 (29%) | 681 | 519 (76%) |
| 12–23 months | 769 | **97** | **69** (71%) | 31 | 13 (42%) | *641* | *472* (74%) |
| 24–35 months | 653 | **171** | **127** (74%) | 23 | 12 (52%) | *459* | *373* (81%) |
| 36–47 months | 615 | **226** | **170** (75%) | 30 | 20 (67%) | *359* | *287* (80%) |
| 48–59 months | 592 | **339** | **260** (77%) | 25 | 17 (68%) | *228* | *195* (86%) |
| All <5 years | 3487 | 976 | 680 (70%) | 143 | 72 (50%) | 2368 | 1846 (78%) |

Cells are in bold or italicised for illustration of the groups used for the calculations reported in the *Results* section of the text.

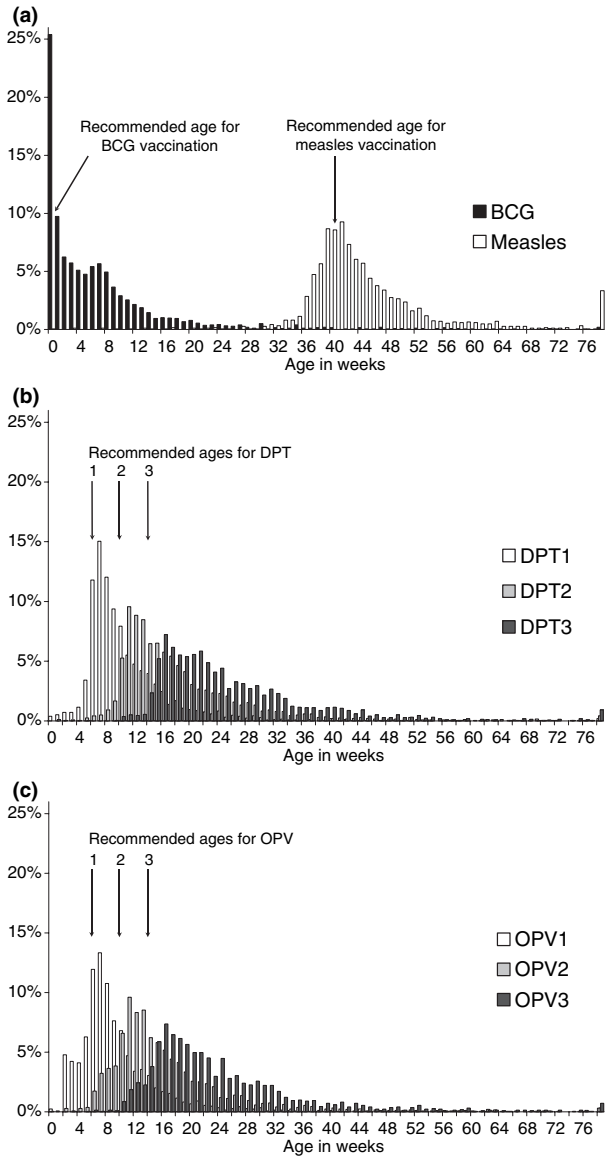


**Figure 2** Age (in weeks) distributions at which BCG (a), DPT (b), OPV and measles (c) vaccinations were actually received. These graphs and corresponding analyses are restricted to children for whom exact date of birth was known. Arrows indicate recommended age for the particular dose.

children had data on birth place. The irregular vaccination schedule was seen in 9% of the 1681 children born at health facilities, but was 1.70 (1.26–2.31) times more likely in the 468 home-born and 1.90 (1.27–2.84) times more likely in the 210 children born at TBA camps. Father's education was known for 1947 children with both vaccines, of which 1938 had data on place of birth. Of these, the irregular vaccination schedule were seen in 20% of the 142 with the lowest, 11% of the 1051 with average and 9% of 745 with the highest education category [OR for a one-unit increase in father's education category = 0.70 (0.55–0.88)].

## Discussion

Despite the remoteness, the Karonga EPI achieved high vaccine coverage between 1999 and 2003. The final coverage of 86% estimated in the survey is plausible and consistent with no confirmed measles cases in the district since 2003. Malawi has been polio-free since 1992. The actual polio and measles vaccine coverage is also affected by campaigns. It is impossible to assess the number and schedule of these doses as vaccinations during campaigns were not documented. This is a problem in many countries.

Direct vaccination coverage estimation from household surveys requires correctly filled vaccination documents available for review as well as exact birth dates for assessment of ages at vaccination. Documents were missing for 37% and exact birth dates for 29% of the 5418 under 5-year-olds in this population. Fewer of the older children and of those without vaccination document had precise birth dates, which was probably due to a combination of poorer parental recall and recording omissions when documents were issued or replaced. Inaccuracies in vaccine date recording on documents were known to occur as some children had to be excluded from the analysis due to vaccination dates prior to a reliable birth date. Almost half of the whole cohort was excluded due to lack of birth date and/or vaccination document, but 64% of children aged 12–23 months had complete data. This age group is generally targeted for coverage surveys.

Routine EPI vaccination coverage estimates for the entire district were 78%, 52% and 77% for 2001, 2002 and 2003, respectively (based on the lowest coverage for BCG, DPT3, OPV3 or measles vaccine), making coverage in the study population higher than in the district as a whole. This is corroborated by the lower under 5 mortality rates observed in the study population (81.4 per 1000 in 2002–2005), compared to the district estimates (145.7 per 1000 for Karonga District from 2000 Malawi DHS; Ndawala 2001; Chirwa *et al.* 2006). Assuming below-average coverage in 2002, higher exclusion rates of older children due to incomplete data might have led to an underestimation of coverage in this study.

Considering loss of documents over time, over 80% of children probably obtained a document, despite the nominal fee. Possession of a vaccination document was associated with parents' education and proximity to an under-5 clinic. Maternal orphans were less likely to have a document than paternal- or non-orphans, underlining the

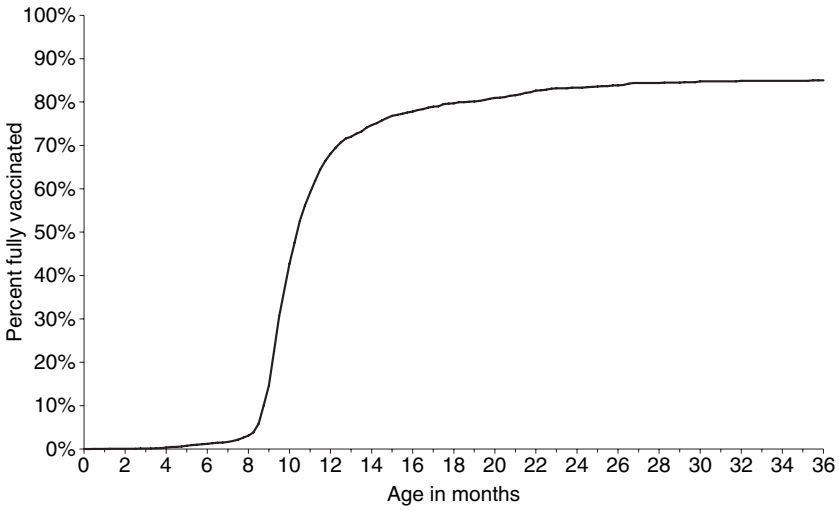


**Figure 3** Kaplan–Meier estimates for age at full vaccination (BCG, DPT3, OPV3 and measles vaccine) for 2744 children born between 1997 and 2004, for whom a precise date of birth and a vaccination document were available (seven were excluded due to inconsistent birth or interview dates).

importance of mothers in ensuring uptake of child health programmes. It is likely that household disruptions following parental deaths would also result in higher loss rates. Proximity to health services and parental education has been reported as important for vaccination coverage in other populations (Cutts *et al.* 1989, 1991).

Although the final cumulative vaccination coverage and equity of access was high, there was a strong association between adherence to vaccination schedule (full coverage by 1 year of age) and birth place, distance to nearest under-5 clinic, maternal education and housing standard. Children with irregular vaccination schedule tended to live further from the nearest under-5 clinic, to have lower standard of housing and to have parents with a lower educational level. Such children would also be expected to have poorer health outcomes and survival, which, without taking into account socio-economic status, could lead to a conclusion that increased mortality was caused by irregular vaccination schedules.

Vaccination delays may be explained by parents bringing their child late to the clinic or by local, national or international vaccine shortages. The fact that some children had received doses of BCG, DPT and measles vaccine more than 12 months late indicates that parents and health staff continued to check and complete the recommended vaccinations. Given the considerable delays in vaccination during the first year of life, any new vaccines targeted at infants (e.g. pneumococcal conjugate vaccine) may not have the desired impact since children may not receive them when they are at greatest risk. It will be important to assess the logistical improvements to the EPI programme required to deliver such vaccines at the optimal ages.

Many children received their last dose of DPT, OPV and measles vaccine several months later than recommended. Approximately half of all children received measles vaccine before 10 months and 17% before the internationally recommended minimum age of 9 months. These 'premature' vaccinations may be a result of date recording errors by the vaccinator. Others may have occurred during local measles vaccination campaigns that were launched following reports of suspected measles cases, although these vaccinations were typically not recorded. Unofficial measles campaigns are no longer encouraged and suspected measles cases have become rare.

Based on BCG scar evidence, a small proportion of BCG vaccinations were not recorded in vaccination documents, either through vaccinator oversight, or loss and replacement of original documents. Early vaccinations are sometimes recorded in the mother's document prior to issue of the child's document. Though vaccinators are advised to transcribe these details into the child health passports, this is sometimes forgotten. Evident date recording errors were rare and the potential bias due to exclusion of these children is small.

Given the claim that DPT given simultaneously with or after measles vaccination might be detrimental to child survival (Breiman *et al.* 2004), it is of interest that 9% of infants in this population had received this schedule. This was associated with indicators of poor socio-economic status, which are likely to confound the effects of vaccination schedules on child survival. The evidence presented challenges the hypothesis of 'non-specific' effects of vaccines on mortality (Aaby *et al.* 2004a,b, 2005a,b; Aaby & Jensen 2005). The ascertainment of vaccination status in this study is broadly comparable with the studies in West

**Table 4** Proportion of children who completed BCG, OPV3, DPT3 and measles vaccine before their first birthday ('fully protected' children) by background characteristics

| | *n* | Fully protected children | Crude OR | Adjusted OR* |
|---|---|---|---|---|
| Total | 1978 | 1323 (67%) | | |
| Age | | | | |
| 12–23 months | 738 | 497 (67%) | Ref. | |
| 24–35 months | 552 | 387 (70%) | 1.14 (0.89–1.44) | |
| 36–47 months | 434 | 285 (66%) | 0.93 (0.72–1.19) | |
| 48–59 months | 254 | 154 (61%) | 0.75 (0.56–1.00) | |
| Sex | | | | |
| Boys | 1031 | 693 (67%) | Ref. | |
| Girls | 947 | 630 (67%) | 0.97 (0.80–1.17) | |
| Place of birth | | | | |
| Health facility | 1375 | 949 (69%) | Ref. | Ref. |
| TBA camp | 197 | 116 (59%) | 0.64 (0.47–0.87) | 0.67 (0.49–0.93) |
| Home | 391 | 248 (63%) | 0.78 (0.62–0.99) | 0.88 (0.68–1.12) |
| Distance to nearest U5-clinic | | | | |
| 0 km | 1155 | 806 (70%) | Ref. | Ref. |
| 1 km | 503 | 335 (67%) | 0.86 (0.69–1.08) | 0.91 (0.72–1.15) |
| 1.5 km | 311 | 178 (57%) | 0.56 (0.44–0.75) | 0.63 (0.48–0.83) |
| Housing standard | | | | |
| 6 (highest) | 59 | 55 (93%) | 6.9 (2.27–19.2) | 0.87† (0.79–0.95) |
| 5 | 58 | 45 (78%) | 1.73 (0.92–3.27) | |
| 4 | 345 | 251 (73%) | 1.33 (1.01–1.77) | |
| 3 | 755 | 503 (67%) | Ref. | |
| 2 | 355 | 222 (63%) | 0.84 (0.64–1.09) | |
| 1 (poorest) | 388 | 237 (61%) | 0.79 (0.61–1.01) | |
| Orphanhood | | | | |
| Non-orphan | 1878 | 1264 (67%) | Ref. | |
| Father died | 53 | 32 (60%) | 0.74 (0.42–1.29) | |
| Mother died | 12 | 5 (42%) | 0.35 (0.11–1.10) | |
| Both died | 0 | | | |
| Mother education | | | | |
| <5 years primary | 237 | 140 (59%) | 0.74 (0.56–0.98) | 0.86 (0.64–1.16) |
| Primary 5+ | 1364 | 903 (66%) | Ref. | Ref. |
| Sec./tert. | 304 | 233 (77%) | 1.68 (1.26–2.24) | 1.45 (1.08–1.96) |
| Father education | | | | |
| <5 years primary | 126 | 83 (66%) | 1.14 (0.77–1.68) | |
| Primary 5+ | 883 | 556 (63%) | Ref. | |
| Sec./tert. | 623 | 446 (72%) | 1.48 (1.19–1.85) | |

*Odds ratios adjusted for all other variables in the model.
†OR for a one-unit change in category assuming a linear trend.

Africa that have been used to generate this hypothesis. Our study provides detailed data on socio-demographic characteristics at the individual and household level and we have demonstrated associations with availability of vaccination documents and delays and deviations in vaccination schedule, that have not been controlled for to this extent in the West African studies.

The Karonga EPI programme has set up an effective network of outreach clinics to facilitate access in the rural areas. In 2003, only 136 of 1955 (7%) scheduled clinics were cancelled due to logistical problems. The relatively densely populated study area has better access to health facilities than other parts of Karonga District. The association of adherence to vaccination schedule with distance to the nearest under-5 clinic and with socio-economic status is likely to play a greater role in the more remote parts of the district.

## Conclusions

Ascertainment of vaccination coverage from a cross-sectional population survey poses considerable difficulties due to incomplete records and lack of precise birth dates. The systematic omission of documenting repeat BCG, measles and polio vaccines during campaigns makes it impossible to determine complete vaccine histories. This

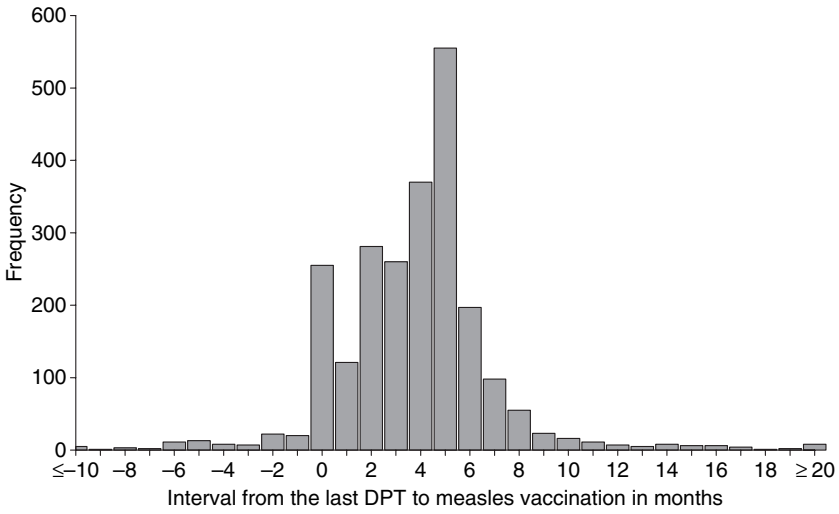


**Figure 4** Distribution of the intervals between the last dose of DPT and measles vaccination in the 2381 children for whom both vaccination dates had been recorded.

study also confirms that analyses based on family-held records are likely to result in misclassification of vaccination status if the absence of vaccination records is interpreted as not having been vaccinated. Adherence to vaccination schedule is strongly influenced by socio-economic characteristics and access to health services, which are intrinsic risk factors for child health and survival. Any analysis of vaccination effects must take account of these variables as potential confounders.

Though the ongoing recording of all deaths in the CRS will allow future analyses of mortality in relation to vaccinations, the difficulties demonstrated in accurate ascertainment of vaccination histories and the complex influence of important confounding factors will pose a problem with any such analyses. A controlled trial would be required to study adequately the implications of different vaccination schedules in this and similar settings.

## Acknowledgements

The Karonga Prevention Study is funded primarily by the Wellcome Trust, with additional support from LEPRA. We thank the Malawi National Health Sciences Research Committee for supporting this work. We thank Professors F. Cutts and F. Schrenk for helpful comments.

## References

Aaby P & Jensen H (2005) Do measles vaccines have non-specific effects on mortality? *Bulletin of the World Health Organization* **83**, 238.

Aaby P, Jensen H, Samb B *et al.* (2003) Differences in female–male mortality after high-titre measles vaccine and association with subsequent vaccination with diphtheria-tetanus-pertussis and inactivated poliovirus: reanalysis of West African studies. *The Lancet* **361**, 2183–2188.

Aaby P, Jensen H, Gomes J *et al.* (2004a) The introduction of diphtheria-tetanus-pertussis vaccine and child mortality in rural Guinea- Bissau: An observational study. *International Journal of Epidemiology* **33**, 374–380.

Aaby P, Jensen H, Rodrigues A, *et al.* (2004b) Divergent female-male mortality ratios associated with different routine vaccinations among female-male twin pairs. *International Journal of Epidemiology* **33**, 367–373.

Aaby P, Jensen H, Benn CS, *et al.* (2005a) Non-specific effects of vaccination: survival bias may explain findings. *British Medical Journal* **330**, 844–845; author reply 845 (2005).

Aaby P, Rodrigues A, Biai S *et al.* (2005b) Vaccines and unexpected observations: flaws or cause for concern? *Vaccine* **23**, 2407–2408.

Breiman RF, Streatfield PK, Phelan M *et al.* (2004) Effect of infant immunisation on childhood mortality in rural Bangladesh: analysis of health and demographic surveillance data. *The Lancet* **364**, 2204–2211.

Chirwa T, Zaba B, Floyd S *et al.* (2006) Demographic analysis of the population of Karonga District, northern Malawi, in the early years of the HIV epidemic (1980–90). *South African Journal of Demography* **10**, 1–24.

Cutts FT, Rodrigues LC, Colombo S *et al.* (1989) Evaluation of factors influencing vaccine uptake in Mozambique. *International Journal of Epidemiology* **18**, 427–433.

Cutts FT, Diallo S, Zell ER *et al.* (1991) Epidemiological investigation of determinants of vaccination in Conakry, Guinea. *International Journal of Epidemiology* **20**, 1099–1106.

Elguero E, Simondon KB, Vaugelade J *et al.* (2005) Non-specific effects of vaccination on child survival? A prospective study in Senegal. *Tropical Medicine and International Health* **10**, 956–960.

Expanded Programme on Immunization (1991) *Training for Mid-level Managers: The EPI Coverage Survey*. World Health Organization, Geneva.

Fine PEM (2000) Commentary: an unexpected finding that needs confirmation or rejection. *British Medical Journal* **321**, 1439.

Global Advisory Committee on Vaccine Safety (2004) Effect of diphtheria–tetanus–pertussis (DTP) vaccination on child survival. *Weekly Epidemiological Record* **29**, 271–272.

Hoshaw-Woodard S (2001) *Description and Comparison of the Methods of Cluster Sampling and Lot Quality Assurance Sampling to Assess Immunization Coverage*. Department of Vaccines and Biologicals, World Health Organization, Geneva.

Jahn A, Crampin AC, Glynn JR *et al.* (2007) Evaluation of a village-informant driven demographic surveillance system in Karonga, Northern Malawi. *Demographic Research* **16**, 219–248.

Kristensen I, Aaby P & Jensen H (2000) Routine vaccinations and child survival: follow up study in Guinea-Bissau, West Africa. *British Medical Journal* **321**, 1435–1438.

Lehmann D, Vail J, Firth MJ *et al.* (2005) Benefits of routine immunizations on childhood survival in Tari, Southern Highlands Province, Papua New Guinea. *International Journal of Epidemiology* **34**, 138–148.

Malawi Ministry of Health and Population (2002) *Expanded Programme on Immunization. Malawi Field Operational Manual*. Malawi Ministry of Health and Population, Malawi.

Moulton LH, Rahmathullah L, Halsey NA *et al.* (2005) Evaluation of non-specific effects of infant immunizations on early infant mortality in a southern Indian population. *Tropical Medicine and International Health* **10**, 947–955.

Ndawala JS (2001) Infant and child mortality. In: *Malawi Demographic and Health Survey 2000* (eds National Statistics Office [Malawi] & ORC Macro). ORC Macro, Zomba, Malawi and Calverton, Maryland, USA, pp. 97–104.

Vaugelade J, Pinchinat S, Guiella G *et al.* (2004) Non-specific effects of vaccination on child survival: prospective cohort study in Burkina Faso. *British Medical Journal* **329**, 1309.

WHO (2001) *Immunization in Practice: Module 2*. Department of Vaccines and Biologicals, WHO, Geneva.

WHO (2003) *State of the World's Vaccines and Immunization*, revised edition. WHO, Geneva.

WHO (2006) Conclusions and recommendations from the Immunisation Strategic Advisory Group. *Weekly Epidemiological Record* **81**, 2–11.

WHO Task Force on Routine Infant Vaccination and Child Survival (2004) *Report of a Meeting to Review Evidence for a Deleterious Effect of DPT Vaccination on Child Survival*. London School of Hygiene & Tropical Medicine, London.

**Corresponding Author** **Andreas Jahn**, Karonga Prevention Study, PO Box 46, Chilumba, Malawi. Fax: +44 (0)20 7636 8739; E-mail: andreas.jahn@lshtm.ac.uk; a_jahn@lighthouse.org.mw